SYNTHETIC ANTIBACTERIAL CLAY COMPOSITIONS AND METHOD OF USING SAME

GOVERNMENT INTEREST

[0001] The invention described herein may be manufactured, used, and licensed by or for the United States Government.

FIELD OF INVENTION

[0002] The present invention relates to synthetic antibacterial compositions having clay-like properties and a method of using these compositions to topically treat bacterially-caused skin infections and skin diseases. The compositions within the scope of the invention comprise a bactericidal effective amount of a reducing agent, such as pyrite, marcasite, pyrrhotite, FeS_2, FeS, $FeSO_4$, or other reducing agents having like properties, and a natural clay or clay mineral and/or a synthetic clay or clay mineral, or other suitable materials having clay-like properties. Divalent iron within the structure of a clay mineral itself may also serve as a reducing agent. It is the presence of the reducing agent in said compositions that renders them antibacterial. The clays or clay minerals serve as a vehicle within which the reducing agent is dispersed, as a dilutent to the reducing agent, and also as an adsorbent and low permeability barrier in use of the composition. These compositions are hydrated so as to form a paste, which is then to be applied to the affected area for treatment. Compositions within the scope of the present invention are suitable to topically treat infections and skin diseases caused by one or more types of bacteria, including antibiotic-resistant bacteria.

BACKGROUND OF THE INVENTION

[0003] Antibiotics are available to treat various types of skin infections. Their route of administration for such treatments can vary. Some are prescribed to be taken orally, some to be applied topically, while others to be administered intravenously. The present invention relates to an antibacterial composition that is to be applied topically to an affected area. In particular, the present invention relates to synthetic antibacterial clay (ABC) compositions.

[0004] The term "antibacterial" is used in the title herein, because an antibacterial clay or clay mineral may either kill bacteria, and therefore be "bactericidal," or render them bacteriostatic, which means that the bacteria cannot grow or reproduce. However, the staining technique used to distinguish between viable and non-viable bacteria herein indicates that most of the bacteria have been killed in the experiments to be described herein, and, therefore, the terms antibacterial and bactericidal are used interchangeably herein. Many agents that are bactericidal also are antimicrobial, which means that the antimicrobial agents may attack bacteria, viruses, protozoa, fungus, etc. Applicants have not yet tested the antibacterial clays against other types of microbes, but speculate that these clays may be effective against some of these entities as well.

[0005] Studies have been conducted exploring the potential use of natural clays in the topical treatment of bacterial infections. For example, certain natural clays have been used in the Ivory Coast to treat Buruli ulcer: see http://fifthkingdom.net/BuruliBusters/default.htm. Although researchers have identified a few natural clays as having bactericidal activity, these studies have not been conclusive as to how or why these clays are effective. Additionally, these studies did not provide definitive guidance as to how one having ordinary skill in the art would conclusively be able to select or identify suitable antibacterial natural clays, or, for that matter, synthesize suitable antibacterial clay-like or clay containing compositions for topical treatment of bacterial infections. Applicants are not aware of any specific guidance present in the art that might direct one skilled in the art to do so. Mechanistically, it has been unclear how these clays produce bactericidal activity.

[0006] According to Williams et al., [Williams et al., "Chemical and Mineralogical Characteristics of French Green Clays Used for Healing," *Clays and Clay Minerals*, Vol. 56, No. 4, 437-452 (2008)], the current accepted treatment of *M. ulcerans* ulcers larger than 5 cm is surgical excision, limb amputation, and/or subsequent skin grafting.

[0007] Certain natural clays have been used in the Ivory Coast to treat Buruli ulcer, a flesh-eating disease caused by *Mycobacterium ulcerans*. This has been documented in O'Hanlon, "Medicinal Clays May Heal Ulcers," *News in Science,* 26 Oct. 2007. This article reports a French clay identified as Agricur* as effective against this flesh-eating disease in Africa's Ivory Coast, and that an interdisciplinary team of microbiologists and mineralogists was attempting to discover how the clay cures. (*Per applicants, although the article references this clay as "Agricur," this clay is correctly referred to as "Argicur," carrying the company/supplier name, Argicur Inc. Le Buisson de Cadouin, France.) The article further indicates that two mineralogically-similar clays had different antibacterial activity. Therefore, based on this article, it appears uncertain which specific clay compositions would be effective for the treatment of bacterial infections. Research was initiated into determining what makes one clay toxic to bacteria and another harmless. The article further indicates that several well-known, pathogenic bacteria—*Salmonella typhimurium, Streptococcus* sp., *Escherichia coli* and *Pseudomonas* sp. —were exposed to the clays; bacterial cultures lost 90-99% (1-2 log unit loss) viability within 24 hours of exposure to French Argicur clays. This was in contrast to only 10-40% reduced viability (0.2-1 log unit loss) caused by other clays or sterile sand. Based on the article, the mechanism as to how the clay works is uncertain. It is also uncertain, based on this article, as to what would make a specific clay more suitable for such treatment, and what would motivate one having ordinary skill in the art to select one clay over another for such treatment.

[0008] Consistent with this article are the results and conclusions set forth in Williams et al., "Killer Clays! Natural antibacterial clay minerals," *Mineralogical Society Bulletin,* 139: 3-8 (2004). The article references and explores the effect on bacteria of two French clays from two different suppliers. The authors reference therein that "[i]t was immediately apparent that one of the clay samples was not effective in killing *Mycobacterium*, but was more suited to promotion of skin granulation after the *Mycobacterium* were killed. These observations remain unexplained." Further, based on the teachings therein, it appeared that one of the clays (Argiletz) apparently kills *Mycobacterium ulcerans* (in human trials); but, in vitro, this same clay enhanced *E. coli*, whereas the Argicur clay killed *E. coli*. Based on the article, much needs to be explored to determine what properties of clay, if any, may render it antibacterial. The authors of the article indicate that they are exploring numerous variables, such as, trace element exchange, surface free energy potential, pH, oxidation state, and how these vary with mineral morphology. No